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위막성 장염 환자에서 의식수준과 내시경 소견과의 연관성

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The Relationship between Endoscopic Features and Unconsciousness in Pseudomembranous Colitis Patients

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Background/Aims: Unconsciousness can create problems in diagnosing and treating pseudomembranous colitis (PMC). While early recognition of clostridium difficile infection and immediate medical therapy can lead to a good prognosis, delayed diagnosis can lead to complex, recurrent and even fatal PMC. The relationships between endoscopic clinical features and unconsciousness are not well documented. The aim of this study was to determine the relationships between PMC endoscopic clinical features and the level of consciousness. **Methods:** Fifty three patients with confirmed PMC during the past 2 years were analyzed retrospectively. Patients were categorized as being in either a conscious state (CS) (i.e. alert) or an unconscious state (US) (i.e. drowsy, stupor, semicoma or coma). Endoscopic patterns of pseudomembranous plaques were classified as grade I=only friability or erosion without plaque, grade II=granular plaque, grade III=nodular plaque, or grade IV=confluent plaque. Clinical features including diagnostic interval (from initial prescription of antibiotic to confirming PMC), endoscopic severity, treatment method, treatment duration and prognosis were compared in between CS and US groups. **Results:** Mean patient age was 65.7±14.9 (male 47.2%, female 52.8%). The overall diagnostic interval was 9.37±4.35 days. Frequently causative antibiotics were cephalosporin (52.8%, 28/53), clindamycin (13.2%, 7/53) and imipenam (9.4%, 5/53). Of the 53 patients, 60.4% (32/53) were categorized as CS, and 39.6% (21/53) as US. In terms of pseudomembranous plaque endoscopic patterns, 18.9% (10/53) were grade I, 28.3% (15/53) were grade II, 32.1% (17/53) were grade III, and 20.8% (11/53) were grade IV. Treatment involved oral administration only. The overall complete treatment rate was 94.3% (50/53). The overall recurrence rate was 5.7% (3/53), and of these one patient died, and two patients were successfully managed by re-treatment. One recurrent and the fatal case occurred in the US group. The US group was positively correlated with longer diagnostic interval, and showed more severe endoscopic features and longer treatment duration compared to the CS group ($p<0.05$). **Conclusions:** Endoscopic and clinical features were more serious in unconscious PMC patients. Compared to conscious patients, unconscious patients being administrated antibiotics must be given greater attention in terms of early diagnosis and successful management of PMC. **(Intestinal Research 2006;4:101-105)**

Key words: Pseudomembranous colitis, Unconsciousness

INTRODUCTION

Since the association between cytotoxins released by Clostridium difficile and antibiotic-induced pseudomembranous colitis (PMC) was reported in 1978,[1,2] C. difficile infection has increased, and is recognized as a primary cause of nosocomial infectious diarrhea.[3,4] The types of antimicrobial agent- and toxin-mediated pathogenesis associated with the pathogenic strain of C. difficile have been well documented. Alterations in the colonic microflora may lead to C. difficile colonization. The main defense mechanisms of the bowel are normal colonic microflora, intestinal motility and immune responses.[5] For unconscious patients in the neurosurgical department, we suspect changes in bowel motility may be an indirect cause

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of PMC. In addition, untreated subjective diarrhea symptoms can be the cause of delayed diagnosis of PMC in patients with neurosurgical problems. While early recognition of C. difficile infection and immediate medical therapy can result in a good prognosis, delayed diagnosis can lead to complex recurrent problems and death. The relationships between endoscopic clinical features and unconsciousness are not well documented. The aim of this study was to determine the relationships between the endoscopic clinical features of pseudomembranous colitis and consciousness level.

PATIENTS AND METHODS

Fifty three patients with confirmed PMC during the past 2 years were analyzed retrospectively. Diagnosis of PMC was confirmed in patients who had received antibiotics within the previous 3 months or whose diarrhea began 72 hours or more after hospitalization. Enzyme immunoassays (EIAs) were used to detect toxin antigen in the stool of patients with typical PMC symptoms such as diarrhea, fever, abdominal pain and leukocytosis. Consciousness levels were categorized as: (1) conscious state (CS)=alert, or (2) unconscious state (US)=drowsy, stupor, semicoma or coma. Endoscopic patterns of pseudomembranous plaques were classified into four grades: (1) grade I=only friability or erosion without plaque; (2) grade II=granular type plaque; (3) grade III=nodular type plaque; and (4) grade IV=confluent type plaque (Fig. 1). The 'diagnostic interval' was defined as the period from initial prescription of antibiotic to confirming PMC. All patients were orally administered metronidazole or vancomycin, including use of a nasogastric tube in unconscious patients. Diagnostic interval, endoscopic severity, treatment method, treatment duration and prognosis were compared between the CS and US groups.

RESULTS

Mean patient age was 65.7±14.89 (male 47.2%, female

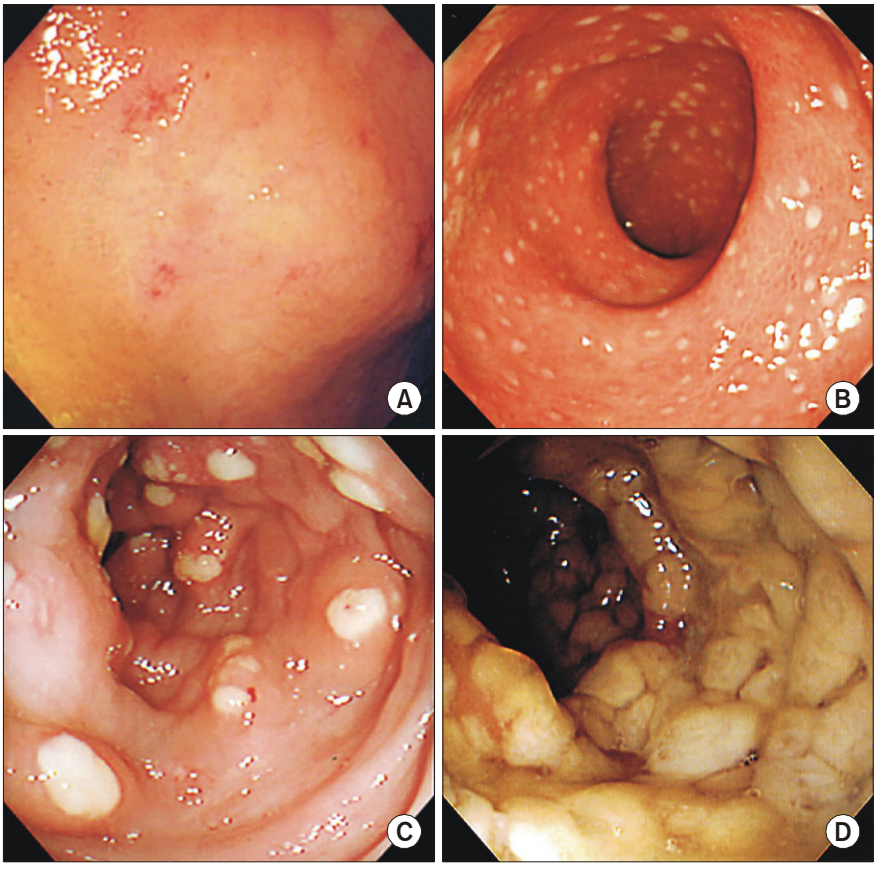

Fig. 1. Grade I; only friability or erosion without plaque (A), grade II; granular plaque (B), grade III; nodular plaque (C) and grade IV; confluent plaque (D).

52.8%). The overall diagnostic interval was 9.37±4.35 days. Frequently causative antibiotics were cephalosporin (52.8%, 28/53), clindamycin (13.2%, 7/53) and imipenam (9.4%, 5/53). Of the 53 patients, 60.4% (32/53) were categorized as CS, and 39.6% (21/53) as US. In terms of pseudomembranous plaque endoscopic patterns, 18.9% (10/53) were grade I, 28.3% (15/53) were grade II, 32.1% (17/53) were grade III, and 20.8% (11/53) were grade IV. Patient characteristics are summarized in Table 1. Treatments comprised only oral administration of either 1,500 mg metronidazole or 500 gm vancomycine.

The mean diagnostic interval was 4.89+3.46 days for the CS group, and 8.81+5.38 days for the US group. Treatment duration was 10.19±3.73 for the CS group, and 13.69±5.68 for the US group. The overall treatment rate was 94.3% (50/53). The overall recurrence rate was 5.7% (3/53), and of these, one patient died, and two were successfully managed by re-treatment. One recurrent and the fatal case were in the US group. Unlike the CS group, the US group showed a positive correlation with more severe endoscopic features ($p<0.05$, Table 2). In addition, the US group showed a longer diagnostic interval and treatment duration ($p<0.05$, Table 3) compared to the CS group. Multivariate stepwise logistic regression analysis revealed that only conscious level was independently and significantly associated with the severity of endoscopic finding (Table 4).

Table 1. Patient Characteristics

Gender	Male	47.2% (25/53)
	Female	52.8% (28/53)
Age (mean±SD)		65.7±14.89
Conscious level	Conscious state	69.8% (37/53)
	Unconscious state	30.2% (16/53)
Causative antibiotics	Cephalosporin	52.8% (28/53)
	Clindamycin	13.2% (7/53)
	Imipenam	9.4% (5/53)
	Quinolone	7.5% (4/53)
	Vancomycin	3.8% (2/53)
	Others	13.2% (7/53)
Endoscopic grades	Grade I	18.9% (10/53)
	Grade II	28.3% (15/53)
	Grade III	17% (32.1/53)
	Grade IV	20.8% (11/53)
Diagnostic interval (mean±SD)		6.08±4.47 days
Treatment regimen	Metronidazole	79.2% (42/53)
	Vancomycin	20.8% (11/53)
Treatment duration (mean±SD)		11.25±4.65 days
Complete response		94.3% (50/53)
Recurrence		5.7% (3/53)

SD, standard deviation.

DISCUSSION

PMC is primarily caused by C. difficile infection. While antibiotics and C. difficile infection have historically been associated with the development of PMC, other risk factors exist for PMC. Most cases of antibiotic-associated diarrhea do not have a definitive cause. C. difficile accounts for only about 20% of all cases of antibiotic-associated diarrhea.[6-8] Factors related to PMC development include

Table 3. The Relation between Conscious Level and Clinical Outcomes

	Diagnostic interval (mean±SD. days)	Treatment duration (mean±SD. days)
Conscious state	4.89±3.36	10.19±3.73
Unconscious state	8.81±5.38	13.69±5.68
p value	<0.01	<0.01

SD, standard deviation.

Table 2. The Relation between Conscious Level and Endoscopic Grades

	Endoscopic grades				p value
	Grade I	Grade II	Grade III	Grade IV	
Conscious state	24.3% (9/37)	35.2% (13/37)	27% (10/37)	13.5% (5/37)	<0.05
Unconscious state	6.2% (1/16)	12.5% (2/16)	43.8% (7/16)	37.5% (6/16)	
Total	18.9% (10/53)	28.3% (15/53)	32.1% (17/53)	20.7% (11/53)	

Table 4. Multi-logistic Regression for Endoscopic Severity

		Endoscopic severity		p value
		Grade I-II (n=25)	Grade III-IV (n=28)	
Age	<50	42.9% (3/7)	57.1% (4/7)	0.560
	≥50	47.9% (22/46)	52.1% (24/46)	
Antibiotics	CEF*	42.8% (12/28)	57.2% (16/28)	0.532
	Others	52% (13/25)	48% (12/25)	
Antibiotics route	IV	42.2% (19/45)	57.8% (26/45)	0.065
	PO	75% (6/8)	25% (2/8)	
Antibiotics duration (days)	<10	46.9% (15/32)	53.1% (17/32)	0.415
	≥10	47.6% (10/21)	52.4% (11/21)	
Diagnostic interval (days)	<6	44.8% (13/29)	55.2% (16/29)	0.322
	≥6	45.5% (10/22)	54.5% (12/22)	
L-tube insertion	No	48.6% (18/37)	51.4% (19/37)	0.136
	Yes	43.8% (7/16)	56.2% (9/16)	
Risk factors	No	50% (22/44)	50% (22/44)	0.230
	Yes	33.3% (3/9)	66.7% (6/9)	
Conscious level	CS†	59.5% (22/37)	40.5% (15/37)	<0.01
	US‡	18.9% (3/16)	81.1% (13/16)	

*CEF, cephalosporin; † CS, conscious state; ‡ US, unconscious state.

host susceptibility or immune function, the virulence of the particular C difficile strain, and the type and timing of antimicrobial exposure.[5] Older age and severity of underlying disease are important risk factors for C. difficile infection. Independent of age, patients with more severe illness are more likely to acquire C. difficile infection. In a study of antibiotic recipients, patients with severe underlying disease at the time of hospital admission were eight times more likely to develop C. difficile infection compared with patients who were less severely ill.[9] Other risk factors include the presence of a nasogastric tube, gastrointestinal procedures, acid antisecretory medications, intensive care unit stay, and duration of hospital stay.[10] There have been no reports suggesting unconsciousness could be a risk factor for PMC.

Infection with C. difficile can produce a wide range of clinical manifestations, including asymptomatic carriage, mild-to-moderate diarrhea, PMC and life-threatening PMC.[6] The host immune response, specifically antitoxin antibody production, may play a role in protecting PMC.[9] The incubation period for PMC after colonization is likely to be less than 1 week, with a median time onset of approximately 2 days.[9,11-13] Most (96%) PMC patients had received antibiotics within 14 days of the onset of diarrhea.[14] Unconsciousness can create problems in diagnosing PMC since unconscious patients can not complain of typical C. difficile diarrhea. More severe disease can present in patients for whom diagnosis is delayed after colonization.

Although sigmoidoscopy and colonoscopy are not indicated for most patients with C. difficile colitis,[6,15] endoscopy is helpful in situations when diagnosis is in doubt or the clinical situation demands rapid diagnosis. The endoscopic findings may be normal in patients with mild diarrhea or may show nonspecific colitis in moderate cases. The finding of colonic pseuodmembranes in patients with antibiotic-associated diarrhea is virtually pathognomonic for C. difficile colitis. Other endoscopic findings include erythema, edema, friability and nonspecific colitis with small ulcerations or erosions.[5] In the present study, unconsciousness was associated with a longer diagnosis interval, more severe endoscopic features typical of PMC, and a longer treatment duration. In unconscious patients, delayed diagnosis results in rapid colonization and more severe PMC. Colorectal motility disorder can be presented in unconscious patients, which limits practical evidences though motility test until now. The finding that endoscopic features were more severe in unconscious patients compare to conscious patients suggests that some motility disorder

related to unconsciousness indirectly can affects PMC prognosis.

Another problem for unconscious patients is the difficulty of oral drug administration. In severe PMC, oral metronidazole or vancomycin is the treatment of choice, with parenteral administration used only until oral agents are tolerated. In unconscious patients, antibiotics have to be administered through a nasogastric tube or retention enema, and the comparative clinical results of these methods are rarely reported. In the present study, all unconscious patients were administered via nasogastric tube, and they were found to require a longer treatment period compared to conscious patients. This observation suggests that gastrointestinal motility disorder and defective immune response in unconscious patients are factors associated with severe PMC.

Practice guidelines for prevention of PMC include limiting the use of antimicrobial drugs, washing hands between patient contact and wearing gloves when in contact with a PMC patient. The present data suggest medical, nursing and other staff must pay even stricter attention to these guidelines when managing unconscious patients as they have additional PMC risk factors.

In conclusion, endoscopic and clinical features were found to be more serious in unconscious PMC patients compared to conscious patients. Unconscious patients who need to be administrated antibiotics must be given addition attention in order to achieve an early PMC diagnosis and successful treatment of the disease.

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